

IN THE CLAIMS

1. (currently amended) Hybrid nanoparticles containing:
a nanosphere, of mean diameter included in the range from 2 to 9 nm, of which at least 90 % by weight consists of Ln_2O_3 where Ln represents a rare earth, optionally doped with a rare earth or an actinide, or a mixture of rare earths, or a rare earth and actinide mixture, in which at least 50 % of the metal ions are rare earth ions,
a coating around the nanosphere chiefly consisting of functionalized polysiloxane, having a mean thickness included in the range from 0.5 to 10 nm, ~~preferably greater than 2 nm and no more than 10 nm~~, and
at least one biological ligand grafted by covalent bonding to the polysiloxane coating.
2. (currently amended) Nanoparticles as in claim 1, characterized in that in the coating from 5 to 75 %, ~~preferably 30 to 50 %~~, of the silicon atoms are bound to four other silicon atoms by oxygen bridges.
3. (currently amended) Nanoparticles as in claim 1, characterized in that the coating has a density included in the range from 1.6 to 2.4, ~~preferably included in the range from 1.8 to 2.1~~.
4. (previously presented) Nanoparticles as in claim 1, characterized in that the coating has a density of less than 2.
5. (previously presented) Nanoparticles as in claim 1, characterized in that between 10 and 100 000 luminescent organic molecules are grafted, by covalent bonding, to the coating.
6. (currently amended) Nanoparticles as in claim 5, characterized in that the luminescent ~~fluorescent~~ organic molecules are chosen from among the derivatives of rhodamine or fluorescein.

7. (previously presented) Nanoparticles as in claim 1, characterized in that the nanosphere, for at least 80 % by weight, consists of a rare earth sesquioxide, optionally doped.

8. (currently amended) Nanoparticles as in claim 7, characterized in that the nanosphere, for at least 80 % by weight, consists of Gd_2O_3 , ~~preferably for at least 90 % by weight.~~

9. (currently amended) Nanoparticles as in claim 7, characterized in that the nanosphere, for at least 80 % by weight, consists of Y_2O_3 , ~~preferably for at least 90 % by weight.~~

10. (previously presented) Nanoparticles as in claim 1, characterized in that the nanosphere is doped with a lanthanide of type Eu, Tb, Er, Nd, Yb, Tm representing from 0.1 to 25 % of the metal cations.

11. (original) Nanoparticles as in claim 10, characterized in that the nanosphere is doped with a lanthanide of type Nd or Yb.

12. (original) Nanoparticles as in claim 10, characterized in that the nanosphere is doped with a lanthanide of type Er.

13. (previously presented) Nanoparticles as in claim 1, characterized in that the nanosphere is doped with at least two different lanthanides representing from 0.1 to 25 % of the metal cations, at least one of these lanthanides being chosen from among Eu and Tb.

14. (previously presented) Nanoparticles as in claim 1, characterized in that more than 10 % of the metal cations of the nanosphere are lanthanide cations having magnetic behaviour, chosen from among Gd, Nd.

15. (previously presented) Nanoparticles as in claim 1, characterized in that more than 50 % of the metal cations of the nanosphere are lanthanide cations having a magnetic behaviour chosen from among Gd, Nd.

16. (currently amended) Nanoparticles as in claim 1, characterized in that from 0.01 % to 50 %, ~~preferably from 0.1 % to 10 %~~, of the metal cations of the nanosphere are uranide cations chosen from among Ac, Th, Pa, Np, U, Pu.

17. (currently amended) Nanoparticles as in claim 1, characterized in that at least 1 %, ~~preferably at least 5 %~~, of the metal cations of the nanosphere having extensive neutron-capture capability, chosen ~~for example~~ from among the isotopes ¹⁵⁷Gd and ²³⁵U.

18. (currently amended) Nanoparticles as in claim 1, characterized in that from 1 to 1000, ~~preferably from 1 to 100~~, molecules of biological ligand are grafted onto the coated by covalent bonding.

19. (previously presented) Nanoparticles as in claim 1, characterized in that less than 10 % by weight of these nanoparticles contain more than two molecules of biological ligand grafted onto the coating.

20. (previously presented) Nanoparticles as in claim 1, characterized in that the grafted biological ligand or ligands are derived from nucleotides, sugars, vitamins, hormones, biotin, streptavidin, or any other organic molecule of interest for biological vectoring.

21. (previously presented) Nanoparticles as in claim 1, characterized in that luminescent molecules or complexing molecules other than the biological ligand(s) are grafted onto the coating.

22. (previously presented) Nanoparticles as in claim 1, characterized in that polar

or charged molecules of organophosphate, quaternary amine types are grafted onto the coating.

23. (currently amended) Nanoparticles as in claim 1, characterized in that molecules of water-soluble polymers having a molecular weight of less than 5000 g/mol, ~~preferably less than 1000~~, e.g. polyethylene glycol or dextran, are grafted onto the coating.

24. (previously presented) Colloidal suspension of hybrid nanoparticles as in claim 1.

25. (withdrawn) Method for preparing hybrid nanoparticles, characterized in that it comprises the following successive steps:

- a) preparing a colloidal suspension of nanospheres, of mean diameter included in the range from 2 to 9 nm consisting, for at least 90 wt.%, of Ln_2O_3 where Ln represents a rare earth optionally doped with a rare earth or an actinide, or a mixture of rare earths, or a rare earth and actinide mixture in which at least 50 % of the metal ions are rare earth ions,
- b) adding to the colloidal suspension the necessary quantity of a mixture of organoalcoxysilane and cross-linking agent to form a coating on the surface of the particles, chiefly consisting of polysiloxane functionalized with at least one reactive group, having a mean thickness included in the range from 0.5 to 10 nm, preferably greater than 2 nm and no more than 10 nm, and
- c) chemically grafting at least one biological ligand to the coating, by coupling with a reactive group present on the coating surface,
- d) optionally separating and drying the hybrid nanoparticles obtained.

26. (withdrawn) Preparation method as in claim 25, characterized in that at step a) a colloidal suspension containing between 100 mg and 100 g of nanospheres per litre of solvent is prepared by dissolving precursors of rare earth and/or actinides in a polar solvent, in particular a polyol of ethyleneglycol type, and heating to a

temperature of between 130 and 250°C, in the presence of the quantity of water at least necessary to form the desired sesquioxide and optionally of a base such as NaOH at a concentration of between 0.01 and 1 mol/l solvent.

27. (withdrawn) Method as in claim 26, characterized in that the precursors of rare earth or actinides are of chloride, acetate or nitrate type.

28. (withdrawn) Method as in claim 25, characterized in that at step b), orthosilicate tetraethyl (TEOS) is used as cross-linking agent.

29. (withdrawn) Method as in claim 25, characterized in that part of the molecules of organoalcoxysilane used are covalently bound to a luminescent molecule.

30. (withdrawn) Method as in claim 25, characterized in that step c) is preceded by a grafting step of luminescent molecules and/or complexing molecules and/or polar or charged molecules and/or molecules of water-soluble polymers, by coupling with a reactive group present on the coating surface.